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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
08/878,348	06/18/97	HEATH	A	2257-1-001

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EXAMINER	
GAMBEL, P	
ART UNIT	**PAPER NUMBER**
1644	18

DATE MAILED: 09/19/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/878348	HUMAN
Examiner	**Group Art Unit**
GAMBEL	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 7/11/00.

☑ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-10, 12, 13, 15-28 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☑ Claim(s) 1-10, 12, 13, 15-28 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s)._____

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other_____

Office Action Summary

DETAILED ACTION

1. Applicant's amendment, filed 7/11/00 (Paper No. 17), has been entered.
Claims 1, 2, 13, 15 and 17 have been amended.
Claims 24-28 have been added.

Claims 1-10, 12, 13, 15-28 are pending and under consideration.

Claims 11 and 14 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 7/11/00 (Paper No. 17). The rejections of record can be found in the previous Office Action (Paper No. 15).

3. Formal drawings and photographs have been submitted which fail to comply with 37 CAR 1.84. Please see the form PTO-948 previously sent in Paper No. 6.
Applicant is reminded to change the Brief Description of the Drawings in accordance with these changes, if necessary.

4. Upon reconsideration of applicant's amended claims, filed 7/11/00 (Paper No. 17); the previous rejection under 35 U.S.C. 112, first paragraph, has been withdrawn.

5. Claims 25 and 27 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "one or more antigens"

Applicant's amendment, filed 7/11/00 (Paper No. 17), directs support 19-20 of the specification for this limitation.

However, the specification as filed does not provide a sufficient written description for "one or more antigens", as currently recited. It appears that applicant may be relying upon a generic disclosure and possibly a single or limited disclosure of pneumococcal antigen(s); however this does not provided sufficient written description and direction and guidance to the "one or more antigens", currently claimed. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

6. Claims 1-10, 12, 13, 22, 23, 28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-10, 12, 13, 22, 23, 28 are indefinite in the recitation of "consisting essentially of" because the metes and bounds of this transitional phrase in the context of the claimed invention is ambiguous and ill-defined.

It is acknowledged that the transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. See MPEP 2111.03

Applicant's arguments, filed 7/11/00 (Paper No. 17) with respect to the prior art appears to be inconsistent with the characteristics of the claimed products.

For example, applicant argues that the prior art relies upon a cytokine in the prior art vaccine compositions/constructs; while the claims recite "consisting essentially of" which would exclude the prior art inclusion of cytokine.

However, dependent claim 13 recites "further comprising at least one cytokine"; which ultimately depends on claim 2 which recites a vaccine "consisting essentially of".

Therefore, it appears that the claimed immunogenic compositions and vaccines can comprise or consist essentially of elements (e.g. cytokines) other than an adjuvant (CD40-specific antibody or CD40L) joined together with an antigen.

Given this apparent inconsistency in the metes and bounds of "consisting essentially of" and a lack of definition in the specification as filed for the metes and bounds of "consisting essentially of"; for examination purposes; the recitation of "consisting essentially of" is interpreted to be the same as "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

B) In addition to the Section (A) above; claim 1 is indefinite in the recitation of "an immunogenic composition" because the claim reads as a compound, given that the adjuvant and antigen are joined together. Minimally, a carrier should be recited, otherwise this reads as a compound per se.

C) The recitation of "an antigen" in claims 27 lacks proper antecedent basis to claim 24.

D) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

7. Claims 1-4, 8-10, 12, 13, 15, 16 and newly added claims 24 and 27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Mond et al. (U.S. Patent No. 5,874,085) essentially for the reasons of record set forth in Paper No. 15.

Applicant's amended claims, filed 7/11/00 (Paper No. 17), have been fully considered but are not found convincing essentially for the reasons of record as well as that set forth in Section 6(A) above.

Applicant argues that there is no disclosure that vaccines include antigens that are joined together with CD40 antibodies or CD40 ligands.

In contrast to applicant's assertions; the prior art complexes which include CD40L also include bound antigen (e.g. see columns 10-11, overlapping paragraph; column 11, lines paragraphs 1 and 4; column 16, Table II).

Applicant argues that column 3, lines 32-34 of the '085 Patent specifically states that that stimulants such as LPS and CD40L activate B cell proliferation and Ig secretion without isotype switching.

This assertion is in contrast to the clear teaching of this Patent ,which is drawn to immunoglobulin class switching (See entire document, including the Summary of the Invention).

Further, the next lines of this Section relied upon by applicant disclose: "These stimulate may permit switching to occur to any of the a number of different isotypes, depending on which the specific stimuli are present. These permissive stimuli include gut are not limited to .... crosslinking of CD40 ligand ... Of these, the most widely studied are ... and direct interaction of CD40 ligand."

Applicant's assertions appear to mischaracterize the prior art teachings with respect to the known ability of CD40 ligand to induce class switching at the time the invention was made.

In addition, products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure; the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Applicant asserts that the claimed immunogenic compositions and vaccines do not require exogenous cytokines.

As pointed out in Section 6(A) above; given the apparent inconsistency in the metes and bounds of "consisting essentially of" and a lack of definition in the specification as filed for the metes and bounds of "consisting essentially of"; for examination purposes; the recitation of "consisting essentially of" is interpreted to be the same as "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

Applicant's arguments are not found persuasive.

8. Claims 1-4, 8-10, 12, 13, 15, 16 and newly added claims 24 and 27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Mond et al. (U.S. Patent No. 5,932,427) for the reasons set forth in Paper No. 15.

Applicant's amended claims, filed 7/11/00 (Paper No. 17), have been fully considered but are not found convincing essentially for the reasons of record as well as that set forth in Section 6(A) above.

Applicant's arguments and the examiner's rebuttal are essentially the same as set forth above in Section 7.

Applicant's arguments are not found persuasive.

9. Claims 1-10, 12, 13, 15-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mond et al. (U.S. Patent No. 5,874,085) AND Mond et al. (U.S. Patent No. 5,932,427) in view of Ledbetter et al.(U.S. Patent No. 5,247,069) and Armitage et al. (U.S. Patent No. 5,961,974) and in view of the art known methods of making and providing vaccine formulations to various antigens at the time the invention was made, as acknowledged by applicant in their traverse response to the restriction requirement, filed 2/27/98 (Paper No. 5), as acknowledged by applicant's specification where it is stated that "it should be apparent to those skilled in the art that this methodology may also be applied to any antigens" (page 7, lines 1-2) for the reasons set forth in Paper No. 15. and that addressed herein.

Applicant's amended claims, filed 7/11/00 (Paper No. 17), have been fully considered but are not found convincing essentially for the reasons of record

Applicant arguments concerning that the prior art is limited to teaching that the CD40L activates B cell proliferation and Ig secretion without isotype switching and that an exogenous cytokine is required for isotype switching has been addressed above in Section 7.
Further applicant's assertions

Applicant argues that the prior art reference Ledbetter et al. discloses that the anti-Bp50 (anti-CD40) antibody could not activate B cells (see column 18, line 21); thereby teachings away from the claimed invention.

As pointed out previously; Ledbetter et al. teaches the use of Bp50-specific antibodies as adjuvants (see entire document, particularly Summary of the Invention, and Section 5.4.1 It was known at the time the invention was made that the Bp50-specific antibodies taught by Ledbetter et al. were specific for CD40, that is, Bp50 and CD40 are the same antigen specificity. Here, Ledbetter et al. also teaches that anti-Bp50 antibodies mimics the activity of other B cell growth factors (columns 19-20, overlapping sentence).

Also, Armitage et al. clearly teach that cross-linked anti-CD40 antibodies are agonistic and that CD40 agonists were useful as vaccine adjuvants (see entire document, including columns 9-10).

Given that the antigen and adjuvant are provided in vivo; such targeting and subsequent signaling of B cells would also be susceptible to other growth factors.

Applicant asserts that there is no reference to the use of antibodies as adjuvant in the formulation of vaccines and that anti-CD40L inhibit B cell proliferation.

It is acknowledged that anti-CD40L antibodies block B cell proliferation, but the claims do not employ such anti-CD40L antibodies. The claims employ anti-CD40 antibodies and the CD40L itself in the claimed immunogenic compositions and vaccines.

Applicant assert that consistently the '974 patent states that anti-CD40 antibodies require IL-4 and cross-linking to mediate B cell proliferation and immunoglobulin secretion (see column 5,. lines 57-62).

In contrast to applicant's assertions; Armitage et al. clearly teach that oligomeric CD40L and cross-linked anti-CD40 antibodies are agonistic and that CD40 agonistic were useful as vaccine adjuvants (see entire document, including columns 9-10).

Applicant asserts that the invention is not an obvious extension of the current immunological dogma. For example, applicant asserts that a conjugate of an anti-CD40 antibody and an antigen would not expected to be effective in enhancing immune responses. Applicant asserts that the antigen-anti-CD40 conjugate would be internalized by antigen processing cells and the processed into short peptides for preparation of MHC Class II presentation and that the anti-CD40 antibody would be proteolyzed along with the antigen in the APC.

The claims do not limit the claimed invention from the use of cross-linking via anti-CD40 antibodies. B cells also serve as antigen presenting cells and the use anti-CD40 antibodies conjugated to antigen would have been expected to serve the dual role of delivering antigen to the appropriate cell type for antigen presentation and antibody production.

Applicant cites Wong et al. (J. Immunol. 162: 2251-2258, 1999) to indicate that the use of CD40L as an adjuvant did not include the step of cross-linking the antigen to CD40L.

However, it was known to the ordinary artisan at the time the invention was made, including the prior art references of record that adjuvants and vaccines comprised various formulations, including providing the adjuvant and antigen separately, together as an composition and joined/linked/conjugated, as well as recombinantly made and expressed.

While Wong et al. Discloses the combination of CD40L and antigen; it does not teach away from other known formulations at the time the invention was made, as asserted by applicant.

With respect to the newly added claim 25 which recites that the a vaccine "does not comprise an exogenous cytokine" and to a possible interpretation of the newly added limitation of "consisting essentially of"; the following is noted.

Given the clear teachings of Armitage et al. that oligomeric CD40L and cross-linked anti-CD40 antibodies are agonistic and that CD40 agonistic were useful as vaccine adjuvants (see entire document, including columns 9-10); it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine agonistic CD40L or anti-CD40 antibody with antigen as a conjugate (or recombinant formulation) in the absence of additional cytokines to induce immune responses to antigens of interest.

Given the clear teachings of both Armitage et al. and Ledbetter et al. that either CD40L or anti-CD40 antibodies serve as cytokines and the art known constructs of conjugating antigen to adjuvant, as taught by Mond et al.; it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine agonistic CD40L or anti-CD40 antibody with antigen as a conjugate (or recombinant formulation) in the absence of additional cytokines to induce immune responses to antigens of interest.

Also, as pointed out above and well known in the art at the time the invention was made; given that the antigen and adjuvant are provided in vivo; such targeting and subsequent signaling of B cells would also be susceptible to other growth factors.

Applicant's arguments are not found persuasive.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
September 18, 2000